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Coronary Artery Disease

Characteristics, Management, and Outcomes of 5,557 Patients Age ≥90 Years With Acute Coronary Syndromes

Results From the CRUSADE Initiative

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Objectives The goal of this work was to explore the treatment and outcomes of patients with non–ST-segment elevation acute coronary syndromes (NSTE-ACS) age ≥90 years.

Background The elderly are often excluded from clinical trials of NSTE-ACS and are underrepresented in clinical registries.

Methods We used data from the CRUSADE registry to study 5,557 patients with NSTE-ACS age ≥90 years and compared their baseline characteristics, treatment patterns, and in-hospital outcomes with a cohort age 75 to 89 years (n = 46,270).

Results Although both groups had much in common, compared with the younger elderly, the older elderly were less likely to be diabetic, smokers, or obese. Among patients without contraindications, the older elderly were less likely to receive glycoprotein IIb/IIIa inhibitors and statins during the first 24 h and were less likely to undergo cardiac catheterization within 48 h. The older elderly were more likely to die (12.0% vs. 7.8%) and experienced more frequent adverse events (26.8% vs. 21.3%) during the hospitalization—differences that persisted after adjustment for baseline patient and hospital characteristics. Increasing adherence to guideline-recommended therapies was associated with both increased bleeding and a graded reduction in risk-adjusted in-hospital mortality across both age groups.

Conclusions In this large population of nonagenarians and centenarians with NSTE-ACS, increasing adherence to guideline-recommended therapies was associated with decreased mortality. These findings reinforce the importance of optimizing care patterns for even the oldest patients with NSTE-ACS, while examining novel approaches to reduce the risk of bleeding in this rapidly expanding patient population. (J Am Coll Cardiol 2007;49:1790–7) © 2007 by the American College of Cardiology Foundation

The elderly are the fastest growing segment of the U.S. population. Whereas other diseases have surpassed heart disease as the primary cause of death at younger ages, heart disease remains the number one killer of elderly patients (1). Although just 2% of the U.S. population is over age 85, this group accounts for 30% of all myocardial infarction-related deaths (2,3). Despite their increasing prevalence and burden of disease, those of extreme chronological age are often excluded from cardiovascular clinical trials, and numbers included in clinical registries remain low. Therefore, little is known about the management and outcomes of acute coronary syndromes in this subgroup. In particular, there is uncertainty regarding the risks and benefits of current treatment guidelines, which have been developed on the basis of observations from predominantly younger populations (4).

As a result of the changing demographics in the U.S., there are now sufficient numbers of older elderly patients (age ≥90 years) in clinical registries to enable an analysis of this unique

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subgroup. The CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the American College of Cardiology/American Heart Association Guidelines) National Quality Improvement Initiative is an ongoing, voluntary, observational data collection and quality improvement initiative among patients with non–ST-segment elevation acute coronary syndromes (NSTE-ACS) and currently includes more than 5,000 patients age ≥90 years (the "older elderly")—representing one of the largest cohorts of such patients ever assembled (5). In this study, we used data from CRUSADE to examine contemporary treatment and outcomes of NSTE-ACS among the older elderly, to compare their treatment and outcomes with those of a "younger elderly" cohort (age 75 to 89 years), and to identify key clinical features associated with adverse outcomes among this understudied population.

Methods

Patient population. The population for our study was derived from the CRUSADE Quality Improvement Initiative. Details of the CRUSADE design and data elements have been published previously (5). To be eligible, patients must arrive at a participating facility either via the emergency department or by transfer within 24 h of onset of symptoms. In addition, their initial evaluation must reveal 1 or more high-risk features including ST-segment depression, transient ST-segment elevation, or elevated levels of cardiac biomarkers. The institutional review board at each hospital approves participation in CRUSADE.

Our analysis included patients age ≥75 years enrolled in CRUSADE from January 1, 2001, through June 30, 2005. During this period, a total of 148,147 patients were enrolled at 525 hospitals. After excluding 255 patients who were missing age data and 96,065 patients age <75, the final population for our analysis included 51,827 patients ≥75 years old, of whom 5,557 were ≥90 years old and 112 were ≥100 years old.

Data collection and definitions. All data were obtained by retrospective chart review by trained data abstractors using standardized case report forms and definitions. Data collected include baseline clinical characteristics, laboratory results, use of acute medications (<24 h from presentation), use and timing of invasive cardiac procedures (e.g., coronary angiography, percutaneous coronary revascularization, bypass surgery), in-hospital clinical outcomes, and discharge medications and interventions. Contraindications to specific therapies were also recorded, details of which are contained in the Appendix.

Post-admission myocardial infarction was defined as clinical signs and symptoms of a new infarction confirmed by new electrocardiogram (ECG) changes or (re-)elevation of cardiac biomarkers. Stroke was defined as a new focal neurologic defect lasting >24 h. Heart failure was defined as exertional dyspnea, orthopnea, rales greater than one-third of lung fields, elevated jugular venous pressure, or pulmonary congestion on chest X-ray thought to be related to cardiac dysfunction. Cardiogenic shock was defined as systolic blood pressure <90 mm Hg for >1 h felt to be secondary to cardiac dysfunction. Major bleeding was defined as an absolute hematocrit drop of ≥12%, intracranial hemorrhage, retroperitoneal bleed, red blood cell transfusion in conjunction with a documented bleeding event if baseline hematocrit was <28%, or any red blood cell transfusion if baseline hematocrit was ≥28%. Any adverse outcome was defined as post-admission myocardial infarction, cardiogenic shock, heart failure, stroke, or death.

Abbreviations and Acronyms

CI = confidence interval

NSTE-ACS = non–ST-segment elevation acute coronary syndromes

OR = odds ratio

Statistical analysis. We compared baseline patient characteristics, clinical presentations, in-hospital care patterns, and in-hospital outcomes between the older elderly population (age ≥90 years) and a younger elderly (age 75 to 89 years) cohort. Continuous variables are described as medians and 25th and 75th percentiles, whereas categorical variables are described as frequencies. For binary comparisons, we used Wilcoxon rank sum tests for continuous variables and chi-square tests were for categorical variables.

Analyses of the association between receipt of 5 guideline-recommended acute therapies (aspirin, beta-blockers, heparin within 24 h of presentation, performance of early cardiac catheterization [i.e., within 48 h of presentation], and glycoprotein IIb/IIIa inhibitors for patients undergoing early cardiac catheterization) and in-hospital outcomes were performed based on both the cohort eligible for at least 1 of the therapies and on the "ideal patient cohort," such that patients with 1 or more contraindications to a therapy were excluded from both the numerator and denominator of the calculation (6). For each patient in the population eligible for at least 1 of the therapies, we then calculated an adherence score equal to the number of therapies received (0 to 5) divided by the number of therapies the patient was eligible to receive (1 to 5). This value was multiplied by 100 to arrive at the percent adherence score. For these and other analyses of in-hospital outcomes, we excluded patients with missing outcome data and those who were transferred to another hospital before discharge.

We also examined the association between major bleeding and receipt of 5 therapies known to be associated with bleeding (aspirin, heparin, clopidogrel within 24 h, early cardiac catheterization, and administration of glycoprotein IIb/IIIa inhibitors for patients undergoing early catheterization). For these analyses, the dependent variable was the number of therapies received (rather than the proportion of eligible therapies). This approach was chosen because we felt that the number of cumulative therapies, rather than proportional adherence, would be more closely related to bleeding outcomes. These analyses were performed using both the overall patient population

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as well as the "ideal patient cohort" method. For the analyses of bleeding complications and transfusion, we also excluded patients who underwent coronary artery bypass surgery during the hospitalization.

To examine the independent association between age group (older elderly vs. younger elderly) and each in-hospital outcome of interest, we used a generalized estimating equation logistic regression approach to account for the effect of potential confounders as well as within-hospital clustering of responses (7). In each case, our multivariable model adjusted for the following covariates: female gender, body mass index, race, family history of coronary artery disease, hypertension, diabetes, current/recent smoker, hypercholesterolemia, prior myocardial infarction, prior percutaneous coronary intervention, prior coronary artery bypass graft, prior heart failure, prior stroke, renal insufficiency, ST-segment depression, ST-segment elevation, both ST-segment depression and ST-segment elevation, signs of heart failure at presentation, heart rate, systolic blood pressure, and positive cardiac biomarkers.

To investigate the independent relationship between adherence to recommended therapies and in-hospital mortality, we used adherence score quartile as a categorical variable with the lowest quartile as the reference group. For this analysis, we tested for a linear trend of adherence score quartile with respect to mortality across age groups and the interaction effects of adherence score quartile and age groups. Similar analyses were performed to explore the relationship between the absolute number of therapies received (as described in the preceding text) and both major bleeding and in-hospital mortality. These analyses were repeated after excluding those patients who died within 24 h of admission (because of their reduced opportunity to receive the therapies). Because our main findings were not altered in these restricted analyses, we report only those results from the overall patient population. Additional analyses were performed to examine the univariate and multivariate associations between receipt of each individual therapy and in-hospital mortality using the identical generalized estimating equation-based approach to risk adjustment as described in the preceding text.

Finally, we performed a multivariable analysis to identify those admission factors independently associated with in-hospital mortality among the older elderly population. Candidate variables for this analysis include all the baseline characteristics listed previously as well as 2-way interaction effects. Although several quantitative interactions were identified, none of the interactions were qualitative, and thus the final model excluded these interactions for ease of interpretation. A p value <0.05 was considered statistically significant for all tests. All analyses were performed with SAS software version 8.2 (SAS Institute Inc., Cary, North Carolina).

Results

Patient characteristics. Baseline characteristics of the older and younger elderly cohorts are described in Table 1. While both groups were similar in many respects, the older elderly ($\geq$90 years) were more likely to be women and were less likely to have traditional coronary artery disease risk factors including diabetes, recent smoking, obesity (defined as body mass index $>$30 kg/m^2), and a family history of premature coronary artery disease (Table 1). There was no difference in low-density lipoprotein cholesterol levels, but the older elderly had lower triglycerides and slightly higher high-density lipoprotein cholesterol levels. The older elderly were more likely to have renal insufficiency and a history of heart failure. The prevalence of previous myocardial infarction did not differ between the 2 groups, but the older elderly were less likely to have undergone previous percutaneous coronary intervention or coronary artery bypass surgery.

Clinical presentation and processes of care. There were only minor differences in clinical presentation between the older and younger elderly (Table 2). The older elderly were somewhat less likely to have ST-segment depression on their presenting ECG but more likely to have elevated cardiac biomarkers. The older elderly were somewhat more likely to have evidence of hemodynamic compromise on presentation including systolic blood pressure $<$90 mm Hg, heart rate $>$100 beats/min, and signs of heart failure on physical exam. The older elderly were less likely to be cared for by a cardiologist (33.0% vs. 48.0%, $p < 0.001$).

Use of guideline-recommended therapies. The proportion of patients with documented contraindications to guideline-recommended therapies is listed in Table 3. While contraindications to aspirin and beta-blockers were similar between the older and younger cohorts, the older elderly more often had documented contraindications to heparin, clopidogrel, angiotensin-converting enzyme inhibitors, statins, and glycoprotein IIb/IIIa inhibitors. Cardiac catheterization was felt to have been contraindicated twice as frequently among the older elderly compared with the younger elderly (59.8% vs. 26.9%, $p < 0.001$)—most commonly due to either "advanced age" (40.6%) and "do-not-resuscitate" status (29.3%).

Even among patients without contraindications, the older elderly were less likely to receive guideline-recommended acute therapies including heparin (75.1% vs. 82.4%), glycoprotein IIb/IIIa inhibitors (12.0% vs. 29.2%), and statins (30.4% vs. 45.7%; all $p < 0.001$) in the first 24 h after admission (Table 4). Among patients not receiving statins before admission, rates of statin use within 24 h of presentation were 18.7% and 26.7% for the older and younger elderly cohorts, respectively ($p < 0.001$). Among eligible patients, only 10.8% of the older elderly compared with 36.3% of the younger elderly underwent cardiac catheterization within the first 48 h after presentation ($p < 0.001$). Accordingly, the use of revascularization was less frequent

Table 1 Baseline Demographics and Clinical Characteristics

	Age ≥90 yrs (n = 5,557)	Age 75–89 yrs (n = 46,270)	p Value
Age (yrs)*	92 (91, 94)	81 (78, 84)	<0.001
Female gender (%)	67.4	50.1	<0.001
White race (%)	86.1	85.7	NS
BMI (kg/m^2)*	23.4 (20.8, 26.6)	25.8 (22.9, 29.2)	<0.001
Diabetes mellitus (%)	20.4	34.2	<0.001
Hypertension (%)	73.7	76.1	0.0001
Hyperlipidemia (%)	24.9	45.2	<0.001
Previous stroke (%)	16.5	15.8	NS
Obesity (BMI ≥30 kg/m^2) (%)	7.6	18.9	<0.001
Previous MI (%)	33.0	33.7	NS
Previous CABG (%)	9.3	23.7	<0.001
Previous PCI (%)	8.7	20.1	<0.001
History of heart failure (%)	39.3	26.9	<0.001
Family history of CAD (%)	14.8	25.0	<0.001
Recent/current smoker (%)	2.5	8.8	<0.001
Previous aspirin use (%)	46.7	49.2	0.001
Creatinine clearance (ml/min)†	23.9 (18.2, 31.6)	36.0 (26.0, 47.6)	<0.001
LDL (mg/dl)*	94.0 (71.0, 119.0)	93.0 (71.0, 118.0)	NS
HDL (mg/dl)*	44.0 (35.0, 54.0)	41.0 (34.0, 51.0)	<0.001
Triglycerides (mg/dl)*	96.0 (69.0, 131.0)	109.0 (77.0, 154.0)	<0.001
Baseline hematocrit (%)*	37.2 (33.6, 40.7)	38.3 (34.4, 41.9)	<0.001
Medicare (%)	73.1	68.9	<0.001
HMO/private (%)	25.4	28.7	<0.001

*Presented as median (25th, 75th percentiles); †creatinine clearance calculated by the Cockgroft-Gault formula.

BMI = body mass index; CABG = coronary artery bypass graft; CAD = coronary artery disease; HDL = high-density lipoprotein; HMO = health maintenance organization; LDL = low-density lipoprotein; MI = myocardial infarction; PCI = percutaneous coronary intervention.

among the older versus younger elderly (12.6% vs. 40.1%, $p < 0.001$).

In-hospital outcomes. Compared with the younger elderly, the older elderly were more likely to die during the hospitalization (12.0% vs. 7.8%, $p < 0.001$) and were also more likely to experience any adverse cardiovascular outcome (26.8% vs. 21.3%, $p < 0.001$) (Table 5). These differences in outcomes persisted after adjustment for potential confounding characteristics with adjusted odds ratios (OR) of 1.23 (95% confidence interval [CI] 1.13 to 1.35) for mortality and 1.08 (95% CI, 1.00 to 1.15) for any adverse outcome. However, the adjusted risks of in-hospital stroke (OR 0.61, 95% CI 0.45 to 0.82) and major bleeding (OR 0.67, 95% CI 0.58 to 0.78) were lower among the older elderly (Table 5). The adjusted ORs were generally similar when the analysis was restricted to the ideal cohort of patients without documented contraindications to guideline-recommended care. Despite their higher rate of adverse outcomes, the older elderly had the same median length of stay (5 days) as the younger elderly.

Table 2 Presenting Characteristics

	Age ≥90 yrs	Age 75–89 yrs	p Value
ST-segment depressions (%)	35.0	36.9	<0.001
CK-MB positive (%)	74.1	71.1	<0.001
CK-MB >5× ULN (%)	29.1	31.6	<0.001
Troponin positive (%)	86.8	81.8	<0.001
Systolic BP <90 mm Hg (%)	4.9	4.1	0.004
Heart rate >100 beats/min (%)	28.9	25.5	<0.001
Signs of heart failure (%)	45.4	33.7	<0.001

BP = blood pressure; CK-MB = creatine kinase-myocardial band; ULN = upper limit of normal.

Figure 1 depicts the relationship between adherence to guideline-recommended therapies and in-hospital mortality across both age groups. As the adherence score increased, the mortality rate declined in a graded fashion ($p < 0.001$ for linear trend) in both groups. At each level of adherence, however, mortality was higher among the older elderly compared with the younger elderly ($p < 0.001$). There was no evidence of a significant adherence score–age interaction. To examine which of the recommended therapies was most closely associated with reduced mortality, we examined risk-adjusted mortality according to the specific therapy received among the ideal cohort of both groups (Table 6). These analyses demonstrated that acute aspirin, beta-blocker, and catheterization within 48 h were all associated with lower adjusted in-hospital mortality. Acute heparin administration was not associated with a reduction in adjusted in-hospital mortality, while use of a glycoprotein IIb/IIIa inhibitor was associated with increased mortality.

Increasing use of therapies with the potential to increase bleeding (acute aspirin, acute clopidogrel, acute heparin, catheterization within 48 h with or without glycoprotein IIb/IIIa inhibitors) was associated with a direct, graded relationship with the risk of major bleeding across both age

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Table 3 Documented Contraindications to Acute Medical Therapies

Medication	Age ≥90 yrs	Age 75–89 yrs	p Value
Aspirin (%)	10.0	7.8	0.52
Beta-blockers (%)	14.0	11.1	0.024
Heparin* (%)	15.0	8.9	<0.001
Clopidogrel (%)	23.3	15.1	<0.001
Angiotensin-converting enzyme inhibitors (%)	20.6	14.6	<0.001
Angiotensin receptor blockers (%)	16.2	8.6	<0.001
Statin (%)	10.9	5.7	<0.001
Glycoprotein IIb/IIIa inhibitors (%)	40.7	22.4	<0.001

*Heparin: low-molecular-weight or unfractionated heparin.

groups, among those eligible for all 5 therapies (Fig. 2). This relationship remained highly statistically significant in analyses that adjusted for differences in baseline patient characteristics ($p < 0.001$ for linear trend).

Multivariable analysis: admission factors associated with mortality. The results of our multivariable analysis to identify admission factors associated with in-hospital mortality are summarized in Table 7. Among the older elderly, traditional coronary disease risk factors (diabetes, renal insufficiency, obesity), acute coronary syndrome severity (troponin ratio), and compromised hemodynamics (higher heart rate, lower systolic blood pressure, signs of heart failure) were each independently associated with increased in-hospital mortality. Prior percutaneous coronary intervention and dyslipidemia were associated with lower in-hospital mortality.

Discussion

In this study, we used data from the CRUSADE initiative to investigate the contemporary treatment and outcomes of NSTE-ACS among one of the largest cohorts of nonagenarians and centenarians ever studied. In-hospital outcomes for the older elderly were poor; 1 in 4 suffered a major adverse outcome, and 1 in 8 did not survive to discharge. Although the older elderly were less likely than their younger elderly counterparts to receive guideline-recommended acute hospital care, there was a strong, graded relationship between receipt of such therapies and lower in-hospital mortality. This relationship was observed despite a graded increase in major bleeding among the older elderly associated with receiving a greater number of antithrombotic and invasive interventions.

The American College of Cardiology/American Heart Association Guidelines for the Management of Unstable Angina and Non–ST-Segment Elevation Myocardial Infarction recognize that elderly patients are at increased risk from coronary revascularization procedures, but nonetheless suggest that the benefits of aggressive treatment and prompt revascularization can be extrapolated from clinical trials that enrolled predominantly younger patients to the older elderly (4). Our findings, which demonstrate a strong, graded association between adherence to guideline-recommend therapies and lower in-hospital mortality among both the younger and older elderly, support this position. In particular, we found that use of aspirin, beta-blockers, and early cardiac catheterization was associated with a marked reduction in the risk of in-hospital mortality among both groups. In practice, however, guideline-recommended acute therapies were more likely to be considered "contraindicated" among those age ≥90 years compared with the 75- to 89-year-old cohort.

For several recommended therapies, including early cardiac catheterization, the most common contraindication cited was advanced age itself. This category likely represents a comprehensive term that includes a broad range of clinical, ethical, and economic factors that are difficult to discern. Do-not-resuscitate status was the next most common contraindication. Do-not-resuscitate status may indicate reluctance on the part of the patient to undergo what are perceived to be futile life-saving efforts, although code status should not preclude optimal medical management (8). In contrast, "patient refusal" was more often listed as a contraindication among those age 75 to 89 years, suggesting that physicians were more likely to approach even borderline candidates for coronary revascularization among the younger elderly.

Table 4 In-Hospital Treatments Among Patients Without Contraindications

Treatment	Age ≥90 yrs	Age 75–89 yrs	p Value
Medical therapies within 24 h of admission			
Aspirin (%)	90.6	91.7	0.01
Beta-blockers (%)	80.7	82.2	0.02
Heparin (%)*	75.1	82.4	<0.001
Glycoprotein IIb/IIIa inhibitors (%)	12.0	29.2	<0.001
Angiotensin-converting enzyme inhibitors (%)	45.3	47.1	0.03
Clopidogrel (%)	35.5	40.1	<0.001
Statins (%)	30.4	45.7	<0.001
Coronary interventions			
Cardiac catheterization ≤48 h (%)	10.8	36.3	<0.001
PCI ≤48 h (%)	6.5	20.2	<0.001
CABG during hospitalization (%)	1.1	9.4	<0.001
Coronary revascularization, any (%)	12.6	40.1	<0.001

*Heparin: low-molecular-weight or unfractionated heparin.
CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.

Table 5 In-Hospital Outcomes

Outcome	Age ≥90 yrs	Age 75–89 yrs	Adjusted Odds Ratio (95% CI)*	Adjusted Odds Ratio (95% CI) Among the "Ideal Cohort"*
Death (%)	12.0	7.8	1.23 (1.13–1.35)	1.36 (1.15–1.60)
Myocardial infarction (%)	3.0	3.5	0.87 (0.75–1.02)	1.08 (0.85–1.37)
Stroke (%)	0.9	1.2	0.61 (0.45–0.82)	0.51 (0.29–0.89)
Heart failure (%)	16.4	12.9	1.07 (0.99–1.16)	1.19 (1.04–1.36)
Cardiogenic shock (%)	3.1	3.5	0.75 (0.64–0.89)	0.85 (0.64–1.13)
RBC transfusion (%)†	12.8	14.1	0.80 (0.72–0.88)	0.92 (0.78–1.08)
Major bleeding (%)†	9.9	13.1	0.67 (0.58–0.78)	0.84 (0.62–1.13)
Any adverse outcome (%)‡	26.8	21.3	1.08 (1.00–1.15)	1.17 (1.04–1.32)

*Reference group for adjusted odds ratio is the age 75 to 89 year-old group; †excluded patients who underwent bypass surgery; ‡any adverse outcome: post-admission myocardial infarction, cardiogenic shock, heart failure, stroke, or death.
CI = confidence interval; RBC = red blood cell.

The older elderly were less likely to receive statins, heparin, glycoprotein IIb/IIIa inhibitors, or coronary revascularization compared with their younger elderly counterparts—even among patients without documented contraindications to such care. There are several potential explanations for the underutilization of guideline-based therapies among the older elderly. For example, the older elderly were less likely to be cared for by a cardiologist; previous studies have documented that patients under the primary supervision of a cardiologist are more likely to undergo coronary angiography and to receive guideline-recommended therapies (9). Alternatively, underuse of antithrombotic therapies including clopidogrel, heparin, and glycoprotein IIb/IIIa inhibitors may reflect physician concern that even among patients without overt contraindications, there is a greater risk of bleeding complications among the older elderly—an assumption that is supported by our data (10). Recent studies suggest that overdosing of antithrombotic therapies also may be an important risk factor for bleeding complications in the elderly, particularly because renal function may be overestimated in such patients (11). Whether more careful attention to weight and renal-based dose reductions or alternative antithrombotic strategies would further improve the safety of care among the older elderly is not known, however.

We found that, independent of other risk factors and comorbid conditions, the older elderly were 23% more likely to die during their hospitalization compared with the younger elderly. End-organ dysfunction on admission (e.g., renal insufficiency, heart failure, and hypotension), as well as diabetes and obesity, were found to be independently associated with in-hospital mortality. In the future, these admission factors might be used to develop risk stratification strategies in prospective studies

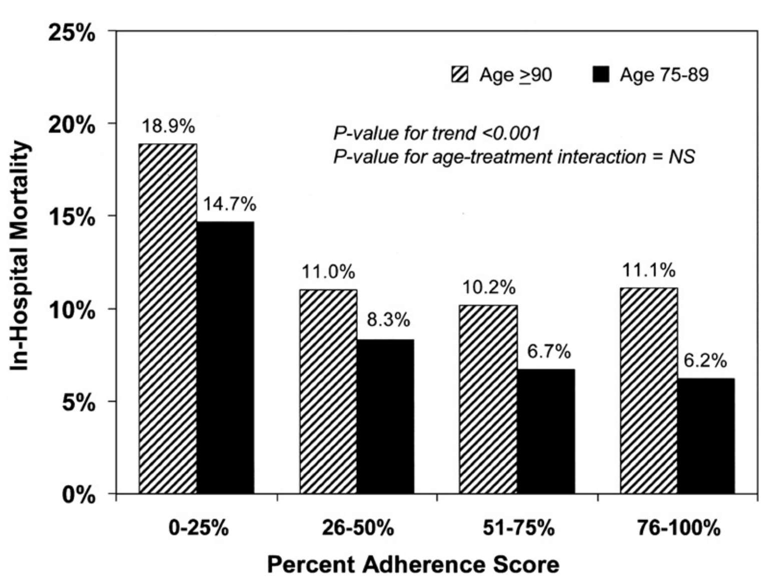

Figure 1 Relationship Between In-Hospital Mortality Across Each Age Group With Increasing Adherence to Recommended Therapies

Guideline-recommended therapies included acute (<24 h) aspirin, acute beta-blockers, acute heparin and cardiac catheterization within 48 h, and receipt of glycoprotein IIb/IIIa inhibitors for patients undergoing early catheterization. Patients who were transferred out were excluded from this analysis.

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Table 6 Odds Ratio of In-Hospital Mortality According to Acute Therapy Received Among Patients Age ≥75 Years

Acute Therapy	Unadjusted OR (95% CI)*	Adjusted OR (95% CI)*
Aspirin	0.57 (0.51–0.64)	0.65 (0.58–0.73)
Beta-blocker	0.61 (0.56–0.67)	0.67 (0.61–0.74)
Heparin†	1.00 (0.91–1.09)	1.06 (0.96–1.17)
Catheterization within 48 h	0.50 (0.46–0.55)	0.70 (0.64–0.77)
Glycoprotein IIb/IIIa inhibitor	1.03 (0.94–1.13)	1.24 (1.12–1.38)
Glycoprotein IIb/IIIa inhibitor and catheterization within 48 h	0.76 (0.68–0.85)	0.94 (0.84–1.06)

*For overall population, excluding those with contraindications or those transferred out; included only patients eligible for each therapy listed. †Heparin: low-molecular-weight or unfractionated heparin.
CI = confidence interval; OR = odds ratio.

Table 7 Multivariable Analysis of Admission Features Associated With In-Hospital Mortality Among the Older Elderly*

Variables	Adjusted OR (95% CI)	Adjusted p Value
Systolic BP (per 10 mm Hg drop)	1.19 (1.16–1.23)	<0.001
Signs of heart failure	1.76 (1.45–2.15)	<0.001
Renal insufficiency	1.48 (1.23–1.78)	<0.001
Troponin ratio (truncated at 40)†	1.01 (1.00–1.02)	<0.001
Diabetes mellitus	1.38 (1.14–1.67)	<0.001
BMI ≥25 kg/m^2 vs. normal BMI‡	1.30 (1.08–1.57)	0.026
BMI <18.5 kg/m^2 vs. normal BMI‡	1.23 (0.89–1.70)	—
Heart rate (per 10 beats/min)	1.05 (1.01–1.08)	0.009
Prior PCI	0.63 (0.45–0.90)	0.010
Dyslipidemia	0.78 (0.65–0.95)	0.014

*Only characteristics with p value <0.05 were included in the adjusted risk model. There were significant quantitative (but not qualitative) interactions between BMI and signs of heart failure as well as prior PCI and signs of heart failure. These terms were not included in the final model. †Troponin ratio: measured troponin/upper limit of normal for local assay at each institution. ‡Normal BMI: 18.5 to 25 kg/m^2.
Abbreviations as in Tables 1, 2, and 6.

that determine the optimal acute therapies for older elderly patients with NSTE-ACS.

Several limitations must be considered when interpreting our findings. Although CRUSADE is community-based and broadly representative, patients in this study were enrolled only if they had chest discomfort and either ECG changes or positive cardiac markers. Thus, many older adults who present with atypical symptoms or with ACS in the setting of another major medical illness (e.g., pneumonia, hip fracture) were excluded. Although we attempted to adjust for a broad range of potential covariates in our multivariate analyses, we cannot discount the possibility of unmeasured confounding—particularly in the relationship between the adherence to guideline-recommended therapies and in-hospital mortality. With respect to the elderly, key variables of functional status, cognitive status, financial considerations, and patient preferences (aside from code status) were not recorded. Furthermore, we were unable to account for undocumented contraindications to recommended therapies or for patients transferred to another hospital. Finally, only in-hospital outcomes were assessed; further studies are necessary to document critical longer-term functional and quality-of-life outcomes of NSTE-ACS among the older elderly.

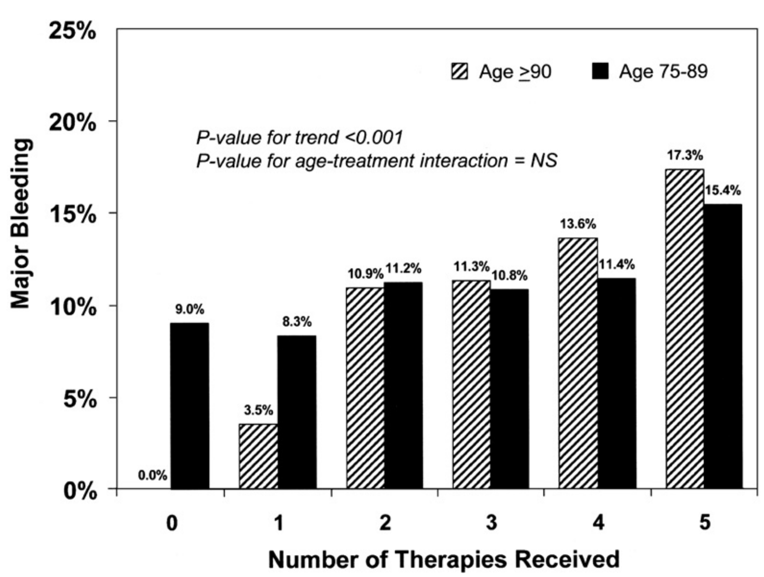

Figure 2 Relationship Between the Number of Therapies Provided and the Incidence of In-Hospital Major Bleeding in Each Group, Including Only the "Ideal Patient Cohort"

Therapies considered included acute (<24 h) aspirin, acute heparin, acute clopidogrel, and catheterization within 48 h with or without the use of glycoprotein IIb/IIIa inhibitors. Patients who were transferred out or who underwent coronary artery bypass surgery during the hospitalization were excluded from this analysis.

Conclusions

In this unselected population of patients with NSTE-ACS, nonagenarians and centenarians were generally similar to their younger elderly counterparts in terms of risk factors and underlying patient characteristics. Despite these similarities, the older elderly were more likely to have documented contraindications to acute treatments, less likely to receive such care independent of contraindications, and were more likely to die in-hospital. Among the older elderly, there was a graded relationship between the number of therapies delivered and bleeding complications. Nonetheless, increasing adherence to guideline-recommended therapies was associated with lower in-hospital mortality in both cohorts. These findings reinforce the importance of optimizing care patterns for even the oldest patients with NSTE-ACS while examining novel approaches to reduce the risk of bleeding for this rapidly expanding patient population.

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APPENDIX

For a list of contraindications to specific therapies, please see the online version of this article.